

PATENT COOPERATION TREATY

PCT

INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY (Chapter II of the Patent Cooperation Treaty)

(PCT Article 36 and Rule 70)

REC'D 06 JUL 2005

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Applicant's or agent's file reference 101002-1 WO	FOR FURTHER ACTION See Form PCT/IPEA/416	
International application No. PCT/SE2004/000417	International filing date (day/month/year) 19.03.2004	Priority date (day/month/year) 22.03.2003
International Patent Classification (IPC) or national classification and IPC A61K 38/05, A61P 7/02, A61P 3/06, A61P 3/10		
Applicant AstraZeneca AB et al		

1. This report is the international preliminary examination report, established by this International Preliminary Examining Authority under Article 35 and transmitted to the applicant according to Article 36.
2. This REPORT consists of a total of 5 sheets, including this cover sheet.
3. This report is also accompanied by ANNEXES, comprising:
 - a. ☐ (sent to the applicant and to the International Bureau) a total of _____ sheets, as follows:
 - ☐ sheets of the description, claims and/or drawings which have been amended and are the basis of this report and/or sheets containing rectifications authorized by this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions).
 - ☐ sheets which supersede earlier sheets, but which this Authority considers contain an amendment that goes beyond the disclosure in the international application as filed, as indicated in item 4 of Box No. I and the Supplemental Box.
 - b. ☐ (sent to the International Bureau only) a total of (indicate type and number of electronic carrier(s)) _____, containing a sequence listing and/or tables related thereto, in computer readable form only, as indicated in the Supplemental Box Relating to Sequence Listing (see Section 802 of the Administrative Instructions).

4. This report contains indications relating to the following items:

- | | | |
|-------------------------------------|--------------|---|
| <input checked="" type="checkbox"/> | Box No. I | Basis of the report |
| <input type="checkbox"/> | Box No. II | Priority |
| <input checked="" type="checkbox"/> | Box No. III | Non-establishment of opinion with regard to novelty, inventive step and industrial applicability |
| <input type="checkbox"/> | Box No. IV | Lack of unity of invention |
| <input checked="" type="checkbox"/> | Box No. V | Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement |
| <input type="checkbox"/> | Box No. VI | Certain documents cited |
| <input type="checkbox"/> | Box No. VII | Certain defects in the international application |
| <input type="checkbox"/> | Box No. VIII | Certain observations on the international application |

Date of submission of the demand 12.10.2004	Date of completion of this report 22.06.2005
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INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY

International application No.

PCT/SE2004/000417

Box No. I Basis of the report

1. With regard to the language, this report is based on the international application in the language in which it was filed, unless otherwise indicated under this item.

- ☐ This report is based on a translation from the original language into the following language _____, which is the language of a translation furnished for the purposes of:
- ☐ international search (under Rules 12.3 and 23.1(b))
 - ☐ publication of the international application (under Rule 12.4)
 - ☐ international preliminary examination (under Rules 55.2 and/or 55.3)

2. With regard to the elements of the international application, this report is based on *(replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report)*:

- ☒ the international application as originally filed/furnished
- ☐ the description:
- pages _____ as originally filed/furnished
- pages* _____ received by this Authority on _____
- pages* _____ received by this Authority on _____
- ☐ the claims:
- pages _____ as originally filed/furnished
- pages* _____ as amended (together with any statement) under Article 19
- pages* _____ received by this Authority on _____
- pages* _____ received by this Authority on _____
- ☐ the drawings:
- pages _____ as originally filed/furnished
- pages* _____ received by this Authority on _____
- pages* _____ received by this Authority on _____
- ☐ a sequence listing and/or any related table(s) – see Supplemental Box Relating to Sequence Listing.

3. ☐ The amendments have resulted in the cancellation of:

- ☐ the description, pages _____
- ☐ the claims, Nos. _____
- ☐ the drawings, sheets/figs _____
- ☐ the sequence listing (*specify*): _____
- ☐ any table(s) related to the sequence listing (*specify*): _____

4. ☐ This report has been established as if (some of) the amendments annexed to this report and listed below had not been made, since they have been considered to go beyond the disclosure as filed, as indicated in the Supplemental Box (Rule 70.2(c)).

- ☐ the description, pages _____
- ☐ the claims, Nos. _____
- ☐ the drawings, sheets/figs _____
- ☐ the sequence listing (*specify*): _____
- ☐ any table(s) related to the sequence listing (*specify*): _____

* If item 4 applies, some or all of those sheets may be marked "superseded."

INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY

International application No.

PCT/SE2004/000417

Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

The questions whether the claimed invention appears to be novel, to involve an inventive step (to be non obvious), or to be industrially applicable have not been examined in respect of:

- ☐ the entire international application
- ☒ claims Nos. 1-3, 15-27, 43

because:

- ☒ the said international application, or the said claims Nos. 15-26, 43
relate to the following subject matter which does not require an international preliminary examination (*specify*):

See PCT Rule 67.1.(iv): Methods for treatment of the human or animal body by surgery or therapy, as well as diagnostic methods.

- ☒ the description, claims or drawings (*indicate particular elements below*) or said claims Nos. 1-3, 27
are so unclear that no meaningful opinion could be formed (*specify*):

This examination is based on the search that has been restricted to melagatran and its prodrugs and the general term "low molecular weight thrombin inhibitor".

- ☐ the claims, or said claims Nos. _____ are so inadequately supported by the description that no meaningful opinion could be formed.
- ☐ no international search report has been established for said claims Nos. _____
- ☐ the nucleotide and/or amino acid sequence listing does not comply with the standard provided for in Annex C of the Administrative Instructions in that:
- | | |
|----------------------------|--|
| the written form | <input type="checkbox"/> has not been furnished |
| | <input type="checkbox"/> does not comply with the standard |
| the computer readable form | <input type="checkbox"/> has not been furnished |
| | <input type="checkbox"/> does not comply with the standard |
- ☐ the tables related to the nucleotide and/or amino acid sequence listing, if in computer readable form only, do not comply with the technical requirements provided for in the Annex C-bis of the Administrative Instructions.
- ☐ See Supplemental Box for further details.

INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY

International application No.

PCT/SE2004/000417

Box No. V Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Claims	<u>4-14, 27-42, 44</u>	YES
	Claims	<u>1-3</u>	NO
Inventive step (IS)	Claims		YES
	Claims	<u>1-14, 27-42, 44</u>	NO
Industrial applicability (IA)	Claims	<u>1-14, 27-42, 44</u>	YES
	Claims		NO

2. Citations and explanations (Rule 70.7)

The claims disclose a use of a low molecular weight thrombin inhibitor for the manufacture of a medicament for use in cholesterol-lowering or lipoprotein-lowering therapy. The claims further disclose a combination of a low molecular weight thrombin inhibitor and a cholesterol-lowering agent. The preferred thrombin inhibitors are melagatran and its prodrugs.

This examination is based on the search that has been restricted to melagatran and its prodrugs and the general term "low molecular weight thrombin inhibitor".

During the search the following documents were found:

A EP 0432 537 A2

B WO 9811896 A1

Document A discloses low molecular weight supersulfated heparins with good antithrombotic activity and a high lipoproteinlipasic activity (see p 2, lines 29-32). It is mentioned in the document that these compounds are "extremely interesting potential antihyperlipemic agents" (see p. 4, lines 25-26). It is also mentioned that pharmaceutical compositions containing the supersulfated heparins are used in the treatment of lipidic metabolism disorders (s p. 4, lines 34-39).

Thus, it is known that low molecular weight thrombin inhibitors can be used in pharmaceutical compositions in the treatment of lipidic metabolism disorders. Hypercholesterolaemia, hyperlipoproteinaemia and hypertriglyceridaemia are different types of lipidic

.../...

Supplemental Box

In case the space in any of the preceding boxes is not sufficient.

Continuation of: BOX V

metabolism disorders.

The difference between the claimed invention and the documents is that melagatran and its prodrugs are preferred in the claimed invention.

It is not shown that the preferred compounds have any new and surprising feature compared the known compounds.

It is considered to be obvious to a person skilled in the art to examine if a low molecular weight thrombin inhibitor can be used in the treatment of different lipidic disorders when it is known that other low molecular weight thrombin inhibitors have this use.

Thus, claims 1-3 are considered not to fulfil the requirements of novelty and inventive step.

Claims 4-14 and 42, 44 are considered to fulfil the requirement novelty but not that of inventive step.

Document B discloses a combination therapy comprised of a cholesterol reducing agent in combination with a platelet aggregation inhibitor. The preferred platelet aggregation inhibitor is a glycoprotein IIb/IIIa receptor antagonist.

The difference between the invention claimed in claims 27-41 and document B is the type of platelet aggregation inhibitor. It has not been shown that the claimed combination shows any unexpected and new feature compared with the known combination.

It is considered to be obvious to a person skilled in the art to examine if a thrombin inhibitor can be used in a combination with a cholesterol-lowering agent when it is known to combine an other type of platelet aggregation inhibitor and a cholesterol-lowering agent.

Thus, claims 27-41 are considered to fulfil the requirement of novelty but not that of inventive step.